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NEWS 16	JUN 30	STN AnaVist enhanced with database content from EPFULL
NEWS 17	JUL 28	CA/CAplus patent coverage enhanced
NEWS 18	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
NEWS 19	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
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NEWS 21	AUG 01	INPADOCDB and INPAFAMDB coverage enhanced
NEWS 22	AUG 13	CA/CAplus enhanced with printed Chemical Abstracts page images from 1967-1998
NEWS 23	AUG 15	CAOLD to be discontinued on December 31, 2008
NEWS 24	AUG 15	CAplus currency for Korean patents enhanced
NEWS 25	AUG 25	CA/CAplus, CASREACT, and IFI and USPAT databases enhanced for more flexible patent number searching
NEWS 26	AUG 27	CAS definition of basic patents expanded to ensure comprehensive access to substance and sequence information

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ocular)
L1        1241 IL(W) 1RA AND (NEUROLOG? OR BRAIN OR EPILEPSY OR HEMORRHAGE OR
               STROKE OR OCULAR)

=> s l1 and py<1997
   1 FILES SEARCHED...
L2         240 L1 AND PY<1997

=> s l1 and treatment
L3         272 L1 AND TREATMENT

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L1         1241 S IL(W)1RA AND (NEUROLOG? OR BRAIN OR EPILEPSY OR HEMORRHAGE OR
L2          240 S L1 AND PY<1997
L3          272 S L1 AND TREATMENT
L4           52 S L3 AND PY<1997

=> dup rem l3
PROCESSING COMPLETED FOR L3
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L5          124 DUP REM L3 (148 DUPLICATES REMOVED)

=> dup rem l4
PROCESSING COMPLETED FOR L4
L6           21 DUP REM L4 (31 DUPLICATES REMOVED)

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     FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 12:06:52 ON 16 SEP 2008
L1         1241 S IL(W)1RA AND (NEUROLOG? OR BRAIN OR EPILEPSY OR HEMORRHAGE OR
L2          240 S L1 AND PY<1997
L3          272 S L1 AND TREATMENT
L4           52 S L3 AND PY<1997
L5          124 DUP REM L3 (148 DUPLICATES REMOVED)
L6           21 DUP REM L4 (31 DUPLICATES REMOVED)

=> display ibib abs l5 1-10

L5   ANSWER 1 OF 124  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2008:96460  CAPLUS
DOCUMENT NUMBER:         148:198623
TITLE:                   Therapeutic protein conjugates with a water-soluble
                         biocompatible, biodegradable polyacetals
INVENTOR(S):             Papisov, Mikhail I.
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 15pp., Cont.-in-part of U.S.
                         Ser. No. 622,998.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  2
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ----------------    ----   --------    --------------------    --------
     US 20080019940       A1    20080124    US 2007-651437          20070109
     US 20040105840       A1    20040603    US 2003-622998          20030718
     US 7160924           B2    20070109
PRIORITY APPLN. INFO.:                      US 2002-397509P     P   20020719
                                            US 2003-622998      A2  20030718
AB   The present invention relates to biodegradable, biocompatible polyacetal
     derivs., and methods for making and using them.  Importantly, the
     polyacetal derivs. can be conjugated to proteins (e.g. hormones,
     antibodies, enzymes) to provide for polyacetal-protein conjugates which
     demonstrate advantages in bioavailability and biocompatibility compared to
     unconjugated proteins, without any undesirable side effects.  The present
     invention further relates to processes for preparing the polyacetal-protein
     conjugates described above.  In a more specific embodiment the polyacetal
     is poly(hydroxymethylene hydroxymethylformal).  The present invention also
     relates to methods of treatment of individuals using the
     polyacetal-protein conjugates as above.  Specifically claimed is a method
     of treating inflammation comprising administering an effective amount of a
     polyacetal-IL-1ra conjugate to a patient in need
     thereof.

L5   ANSWER 2 OF 124     MEDLINE on STN                 DUPLICATE 1
ACCESSION NUMBER:   2008491960     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 18495787
TITLE:              Activation of NOD2 in vivo induces IL-1beta production in
                    the eye via caspase-1 but results in ocular
```

inflammation independently of IL-1 signaling.
AUTHOR: Rosenzweig H L; Martin T M; Planck S R; Galster K; Jann M M; Davey M P; Kobayashi K; Flavell R A; Rosenbaum J T
CORPORATE SOURCE: Department of Ophthalmology, Oregon Health and Science University, 3181 S.W. Sam Jackson Park Rd., Mail Stop: L467 IM, Portland, OR 97239, USA.. rosenzwh@ohsu.edu
CONTRACT NUMBER: EY006484 (United States NEI)
EY013093 (United States NEI)
EY015137 (United States NEI)
F32-EY017254 (United States NEI)
SOURCE: Journal of leukocyte biology, (2008 Aug) Vol. 84, No. 2, pp. 529-36. Electronic Publication: 2008-05-21.
Journal code: 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200809
ENTRY DATE: Entered STN: 5 Aug 2008
Last Updated on STN: 5 Sep 2008
Entered Medline: 4 Sep 2008

AB Nucleotide-binding and oligomerization domain 2 (NOD2) belongs to the emerging Nod-like receptor (NLR) family considered important in innate immunity. Mutations in NOD2 cause Blau syndrome, an inherited inflammation of eye, joints, and skin. Mutations in a homologous region of another NLR member, NALP3, cause autoinflammation, wherein IL-1beta plays a critical role. Here, we tested the hypothesis that IL-1beta is a downstream mediator of NOD2-dependent ocular inflammation. We used a mouse model of NOD2-dependent ocular inflammation induced by muramyl dipeptide (MDP), the minimal bacterial motif sensed by NOD2. We report that MDP-induced ocular inflammation generates IL-1beta and IL-18 within the eye in a NOD2- and caspase-1-dependent manner. Surprisingly, two critical measures of ocular inflammation, leukocyte rolling and leukocyte intravascular adherence, appear to be completely independent of IL-1 signaling effects, as caspase-1 and IL-1R1-deficient mice still developed ocular inflammation in response to MDP. In contrast to the eye, a diminished neutrophil response was observed in an in vivo model of MDP-induced peritonitis in caspase-1-deficient mice, suggesting that IL-1beta is not essential in NOD2-dependent ocular inflammation, but it is involved, in part, in systemic inflammation triggered by NOD2 activation. This disparity may be influenced by IL-1R antagonist (IL-1Ra), as we observed differential IL-1Ra levels in the eye versus plasma at baseline levels and in response to MDP treatment. This report reveals a new in vivo function of NOD2 within the eye yet importantly, distinguishes NOD2-dependent from NALP3-dependent inflammation, as ocular inflammation in mice occurred independently of IL-1beta.

L5 ANSWER 3 OF 124 EMBASE
ACCESSION NUMBER: 2008243927 EMBASE
TITLE: Effects of estrogen on temporal expressions of IL-1β and IL-1ra in rat organotypic hippocampal slices exposed to oxygen-glucose deprivation.
AUTHOR: Choi, Ji-Seung; Kim, Soo-Jung; Shin, Jin A.; Lee, Kyung-Eun; Park, Eun-Mi (correspondence)
CORPORATE SOURCE: Department of Pharmacology, Ewha Medical Research Institute, School of Medicine, 911-1 Mok6dong, Yangcheon-gu, Seoul, 158-710, Korea, Republic of.

empark@ewha.ac.kr
SOURCE: Neuroscience Letters, (20 Jun 2008) Vol. 438, No. 2, pp. 233-237.
Refs: 32
ISSN: 0304-3940 CODEN: NELED5
PUBLISHER IDENT.: S 0304-3940(08)00501-6
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Jul 2008
Last Updated on STN: 2 Jul 2008

AB Anti-inflammatory action of estrogen is involved in neuroprotection but the effects of estrogen on IL-1β and its endogenous antagonist (IL-1ra) have not been clearly defined in the ischemic brain. This study was performed to evaluate whether estrogen affects the expression of IL-1β or IL-1ra and the ratio of the two in the ischemic hippocampus. Rat organotypic hippocampal slices were treated with 17β estradiol (E2, 1 nM) for 7 days, exposed to oxygen-glucose deprivation (OGD) for 30 min, and then reperfused for 72 h. CA1 neuronal death quantified by propidium iodide (PI) staining and expressions of IL-1β and IL-1ra in slices measured by real-time PCR and Western blotting were examined. PI intensities in CA1 in slices treated with E2 were significantly reduced at 24 h and 72 h post-OGD, and IL-1β mRNA expressions were reduced at 6 h and 24 h post-OGD. In addition, IL-1ra mRNA was significantly overexpressed and the ratio of IL-1β to IL-1ra mRNA expression was reduced by E2 especially at 24 h. In terms of protein levels, E2 downregulated IL-1β but upregulated IL-1ra and thereby decreased the IL-1β/ IL-1ra ratio at 24 h. These findings demonstrate that estrogen-induced protection is associated with a decrease in IL-1β and an increase in IL-1ra expression in the ischemic hippocampus during early reperfusion periods, which suggests that modulation of IL-1β/ IL-1ra might be a part of anti-inflammatory effects of estrogen. .COPYRGT. 2008 Elsevier Ireland Ltd. All rights reserved.

L5 ANSWER 4 OF 124 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2007747852 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17965029
TITLE: Besifloxacin, a novel fluoroquinolone antimicrobial agent, exhibits potent inhibition of pro-inflammatory cytokines in human THP-1 monocytes.
AUTHOR: Zhang Jin-Zhong; Ward Keith W
CORPORATE SOURCE: Global Preclinical Development, Bausch & Lomb, 1400 North Goodman Street, Rochester, NY 14603, USA.. jinzhong.zhang@bausch.com
SOURCE: The Journal of antimicrobial chemotherapy, (2008 Jan) Vol. 61, No. 1, pp. 111-6. Electronic Publication: 2007-10-25.
Journal code: 7513617. E-ISSN: 1460-2091.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200802
ENTRY DATE: Entered STN: 19 Dec 2007

Last Updated on STN: 29 Feb 2008
Entered Medline: 28 Feb 2008

AB OBJECTIVES: This study was conducted to evaluate the anti-inflammatory effects of besifloxacin, a novel fluoroquinolone under clinical evaluation for treatment of ophthalmic infections. METHODS: Cytokine expression in human THP-1 monocytes was stimulated by lipopolysaccharide (LPS), and Luminex technology was used to determine the effect of besifloxacin on LPS-induced cytokine expression. Moxifloxacin, a marketed fluoroquinolone used in ophthalmic infections, was used as the control. RESULTS: LPS induced measurable cytokine expression for 14 of the 16 cytokines assayed. Besifloxacin significantly inhibited LPS-stimulated cytokine production in a dose-dependent manner, with a comparable [granulocyte macrophage colony-stimulating factor (GM-CSF), interleukin (IL)-1beta, IL-8, interferon-inducible protein (IP-10), monocyte chemotactic protein-1 (MCP-1) and macrophage inflammatory protein-1alpha (MIP-1alpha)] or better [granulocyte CSF (G-CSF), IL-1alpha, IL-1 receptor antagonist (IL-1ra) and IL-6] potency compared with moxifloxacin. A significant inhibitory effect of besifloxacin was observed at 0.1 mg/L for IL-1alpha, at 1 mg/L for G-CSF, IL-1ra and IL-6 and at 30 mg/L for GM-CSF, IL-12p40, IL-1beta, IL-8, IP-10, MCP-1 and MIP-1alpha. CONCLUSIONS: Besifloxacin acts as an anti-inflammatory agent in monocytes in vitro; this attribute may enhance its efficacy in ocular infections with an inflammatory component and warrants further investigation.

L5 ANSWER 5 OF 124 MEDLINE on STN
ACCESSION NUMBER: 2008346686 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18489763
TITLE: Plasma IP-10, apoptotic and angiogenic factors associated with fatal cerebral malaria in India.
AUTHOR: Jain Vidhan; Armah Henry B; Tongren Jon E; Ned Renee M; Wilson Nana O; Crawford Sara; Joel Pradeep K; Singh Mrigendra P; Nagpal Avinash C; Dash A P; Udhayakumar Venkatachalam; Singh Neeru; Stiles Jonathan K
CORPORATE SOURCE: National Institute of Malaria Research (ICMR), Jabalpur, India.. vidhanjain78@yahoo.com
CONTRACT NUMBER: R21TW006804-01 (United States FIC)
RR03034 (United States NCRR)
SO6GM08248 (United States NIGMS)
SOURCE: Malaria journal, (2008) Vol. 7, pp. 83. Electronic Publication: 2008-05-19.
Journal code: 101139802. E-ISSN: 1475-2875.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200806
ENTRY DATE: Entered STN: 31 May 2008
Last Updated on STN: 1 Jul 2008
Entered Medline: 30 Jun 2008

AB BACKGROUND: Plasmodium falciparum in a subset of patients can lead to cerebral malaria (CM), a major contributor to malaria-associated mortality. Despite treatment, CM mortality can be as high as 30%, while 10% of survivors of the disease may experience short- and long-term neurological complications. The pathogenesis of CM is mediated by alterations in cytokine and chemokine homeostasis, inflammation as well as vascular injury and repair processes although their roles are not fully understood. The hypothesis for this study is that CM-induced changes in inflammatory, apoptotic and angiogenic factors

mediate severity of CM and that their identification will enable development of new prognostic markers and adjunctive therapies for preventing CM mortalities. METHODS: Plasma samples (133) were obtained from healthy controls (HC, 25), mild malaria (MM, 48), cerebral malaria survivors (CMS, 48), and cerebral malaria non-survivors (CMNS, 12) at admission to the hospital in Jabalpur, India. Plasma levels of 30 biomarkers ((IL-1beta, IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-8, IL-9, IL-10, IL-12 (p70), IL-13, IL-15, IL-17, Eotaxin, FGF basic protein, G-CSF, GM-CSF, IFN-gamma, IP-10, MCP-1 (MCAF), MIP-1alpha, MIP-1beta, RANTES, TNF-alpha, Fas-ligand (Fas-L), soluble Fas (sFas), soluble TNF receptor 1 (sTNF-R1) and soluble TNF receptor 2 (sTNFR-2), PDGF bb and VEGF)) were simultaneously measured in an initial subset of ten samples from each group. Only those biomarkers which showed significant differences in the pilot analysis were chosen for testing on all remaining samples. The results were then compared between the four groups to determine their role in CM severity. RESULTS: IP-10, sTNF-R2 and sFas were independently associated with increased risk of CM associated mortality. CMNS patients had a significantly lower level of the neuroprotective factor VEGF when compared to other groups ($P < 0.0045$). The ratios of VEGF to IP-10, sTNF-R2, and sFas distinguished CM survivors from non survivors ($P < 0.0001$). CONCLUSION: The results suggest that plasma levels of IP-10, sTNF-R2 and sFas may be potential biomarkers of CM severity and mortality. VEGF was found to be protective against CM associated mortality and may be considered for adjunctive therapy to improve the treatment outcome in CM patients.

L5 ANSWER 6 OF 124 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:1033092 CAPLUS
TITLE: Interleukin-1 and corticotropin-releasing factor receptors in the hypothalamic-pituitary-adrenal axis
AUTHOR(S): Takao, Toshihiro; Hashimoto, Kozo; De Souza, Errol B.
CORPORATE SOURCE: Division of Community Medicine, Department of Community Nursing, Kochi Medical School, Nankoku, 783-8505, Japan
SOURCE: Neuroimmune Biology (2008), 6(Cytokines and the Brain), 39-54
CODEN: NBEIAQ; ISSN: 1567-7443
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interleukin-1 (IL-1) receptors were localized in mouse brain and pituitary using [125I]IL-1α and [125I] IL-1ra as radioligands. Receptor autoradiog. and in situ hybridization studies demonstrated high densities and a discrete localization of IL-1 receptors and receptor mRNA, resp., in the dentate gyrus of the hippocampus, choroid plexus, and anterior pituitary. Ether-laparotomy stress in mice resulted in a significant increase in [125I]IL-1α binding in the pituitary with no significant alterations observed in the brain; in contrast, [125I]oCRF binding in the pituitary was significantly decreased after the ether-laparotomy stress. The upregulation of IL-1 receptors in the mouse pituitary gland following ether-laparotomy stress was attenuated in a dose-dependent manner by systemic administration of corticotropin-releasing factor (CRF) receptor antagonist D-Phe12-Nle21,38 human CRF(12-41)NH2. Moreover, i.p. injection of r/h CRF resulted in a dramatic increase in [125I]IL-1α binding in the pituitary at 2 and 6 h after the injection although it did not affect [125I]IL-1α binding in the hippocampus. Pretreatment with the nonpeptide, type 1 selective CRF antagonist, CRA 1000 significantly decreased ether-laparotomy stress-induced increases of IL-1R1 mRNA levels in the pituitary. Moreover, ether-laparotomy caused a significant increase of IL-1R1 mRNA in the pituitary of wild-type mice, and this increment of IL-1R1 mRNA in the pituitary was abolished in the CRF knockout (KO) mouse group. The

treatment of AtT-20 mouse pituitary adenoma cells for 24 h with neuroendocrine mediators of stress such as CRF and catecholamine receptor (β2 adrenergic) agonists produced a dose-dependent increase in cAMP and [125I]IL-1α binding.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 2008333360 EMBASE

TITLE: Trimethyltin-evoked apoptosis of murine hippocampal granule neurons is accompanied by the expression of interleukin-1beta and interleukin-1 receptor antagonist in cells of ameboid phenotype, the majority of which are NG2-positive.

AUTHOR: Fiedorowicz, Anna; Figiel, Izabela (correspondence); Zaremba, Malgorzata; Dzwonek, Karolina; Oderfeld-Nowak, Barbara

CORPORATE SOURCE: Laboratory of Mechanisms of Neurodegeneration and Neuroprotection, Department of Molecular and Cellular Neurobiology, Nencki Institute of Experimental Biology, Pasteur 3 Street, 02-093 Warsaw, Poland. i.figiel@nencki.gov.pl

AUTHOR: Schliebs, Reinhard

CORPORATE SOURCE: Laboratory of Neurochemistry, Paul Flechsig Institute for Brain Research, Leipzig, Germany.

SOURCE: Brain Research Bulletin, (5 Sep 2008) Vol. 77, No. 1, pp. 19-26.
Refs: 48
ISSN: 0361-9230 CODEN: BRBUDU

PUBLISHER IDENT.: S 0361-9230(08)00036-1

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 026 Immunology, Serology and Transplantation
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 12 Aug 2008
Last Updated on STN: 12 Aug 2008

AB Interleukin-1beta (IL-1β) has been implicated in various neuropathologies, while IL-1 receptor antagonist (IL-1ra) has been shown to reduce neuronal injury. We investigated the pattern of expression of both cytokines in murine hippocampus after trimethyltin (TMT) intoxication. Using a ribonuclease protection assay, we demonstrated induction of transcription of IL-1β and IL-1ra 3 days following TMT treatment which correlated with the peak of neuronal apoptosis. At this time, immunocytochemical staining revealed enhanced expression of both cytokines in NG2 proteoglycan expressing ameboid cells located at the site of neurotoxic insult, some of which bound also the microglial marker, lectin. There was some overlap between NG2 and lectin staining. Our results suggest that the two cytokines are involved in apoptotic processes in dentate granule cells and indicate that the pro-apoptotic effect of IL-1β prevails over the presumed protective action of IL-1ra. The novel finding of expression of both cytokines in NG2(+) cells of ameboid phenotype indicates that these cells, through the regulatory roles of pro- and anti-inflammatory cytokines, may be involved in control of neuronal death or survival after injury. .COPYRGT. 2008 Elsevier Inc. All rights reserved.

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reserved on STN DUPLICATE 3

ACCESSION NUMBER: 2008261712 EMBASE
TITLE: Plasma IP-10, apoptotic and angiogenic factors associated with fatal cerebral malaria in India.
AUTHOR: Jain, Vidhan; Singh, Mrigendra P.; Singh, Neeru
CORPORATE SOURCE: National Institute of Malaria Research (ICMR), Jabalpur, India. mrigendrapal@gmail.com; vidhanjain78@yahoo.com; oicmrc@yahoo.co.in
AUTHOR: Armah, Henry B.; Wilson, Nana O.; Stiles, Jonathan K.
CORPORATE SOURCE: Department of Microbiology, Biochemistry and Immunology, Morehouse School of Medicine, Atlanta, GA, United States. nwilson@msm.edu; jstiles@msm.edu; hbaarmah@hotmail.com
AUTHOR: Tongren, Jon E.; Ned, Renee M.; Crawford, Sara; Udhayakumar, Venkatachalam
CORPORATE SOURCE: Malaria Branch, Division of Parasitic Diseases, National Center for Zoonotic, Vector-Borne and Enteric Diseases, Atlanta, GA, United States. vxu0@cdc.gov; sgv0@cdc.gov; rin1@cdc.gov; Eric.Tongren@maine.gov
AUTHOR: Joel, Pradeep K.; Nagpal, Avinash C.; Dash, A.P.
CORPORATE SOURCE: Nethaji Subash Chandra Bose Hospital, Jabalpur, Madhyapradesh, India. avinash.nagpal@reiffmail.com; apdash2@rediffmail.com; pradeepj@rediffmail.com
AUTHOR: Stiles, J. K. (correspondence)
CORPORATE SOURCE: Department of Microbiology, Biochemistry and Immunology, Morehouse School of Medicine, Atlanta, GA, United States. jstiles@msm.edu
SOURCE: Malaria Journal, (2008) Vol. 7. arn. 83.
Refs: 62
E-ISSN: 1475-2875
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jun 2008
Last Updated on STN: 27 Jun 2008
AB Background. Plasmodium falciparum in a subset of patients can lead to cerebral malaria (CM), a major contributor to malaria-associated mortality. Despite treatment, CM mortality can be as high as 30%, while 10% of survivors of the disease may experience short- and long-term neurological complications. The pathogenesis of CM is mediated by alterations in cytokine and chemokine homeostasis, inflammation as well as vascular injury and repair processes although their roles are not fully understood. The hypothesis for this study is that CM-induced changes in inflammatory, apoptotic and angiogenic factors mediate severity of CM and that their identification will enable development of new prognostic markers and adjunctive therapies for preventing CM mortalities. Methods. Plasma samples (133) were obtained from healthy controls (HC, 25), mild malaria (MM, 48), cerebral malaria survivors (CMS, 48), and cerebral malaria non-survivors (CMNS, 12) at admission to the hospital in Jabalpur, India. Plasma levels of 30 biomarkers ((IL-1β, IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-8, IL-9, IL-10, IL-12 (p70), IL-13, IL-15, IL-17, Eotaxin, FGF basic protein, G-CSF, GM-CSF, IFN-γ, IP-10, MCP-1 (MCAF), MIP-1α, MIP-1β, RANTES, TNF-α, Fas-ligand (Fas-L), soluble Fas (sFas), soluble TNF receptor 1 (sTNF-R1) and soluble TNF receptor 2 (sTNFR-2), PDGF bb and VEGF)) were simultaneously measured in an initial subset of ten samples from each group. Only those biomarkers which showed significant differences in the pilot analysis were chosen for testing on all remaining samples. The results were then compared between

the four groups to determine their role in CM severity. Results. IP-10, sTNF-R2 and sFas were independently associated with increased risk of CM associated mortality. CMNS patients had a significantly lower level of the neuroprotective factor VEGF when compared to other groups ($P < 0.0045$). The ratios of VEGF to IP-10, sTNF-R2, and sFas distinguished CM survivors from non survivors ($P < 0.0001$). Conclusion. The results suggest that plasma levels of IP-10, sTNF-R2 and sFas may be potential biomarkers of CM severity and mortality. VEGF was found to be protective against CM associated mortality and may be considered for adjunctive therapy to improve the treatment outcome in CM patients.

L5 ANSWER 9 OF 124 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2007572499 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17763411
TITLE: Pattern of interleukin-1beta secretion in response to lipopolysaccharide and ATP before and after interleukin-1 blockade in patients with CIAS1 mutations.
AUTHOR: Gattorno Marco; Tassi Sara; Carta Sonia; Delfino Laura; Ferlito Francesca; Pelagatti Maria Antonietta; D'Osualdo Andrea; Buoncompagni Antonella; Alpigiani Maria Giannina; Alessio Maria; Martini Alberto; Rubartelli Anna
CORPORATE SOURCE: Second Division of Pediatrics, IRCCS, Istituto G. Gaslini, Genoa, Italy.. marcogattorno@ospedale-gaslini.ge.it
SOURCE: Arthritis and rheumatism, (2007 Sep) Vol. 56, No. 9, pp. 3138-48.
Journal code: 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200711
ENTRY DATE: Entered STN: 27 Sep 2007
Last Updated on STN: 8 Dec 2007
Entered Medline: 27 Nov 2007
AB OBJECTIVE: To examine the synthesis, processing, and secretion of interleukin-1beta (IL-1beta), as well as the clinical and biologic effects of IL-1 blockade, in patients with chronic infantile neurologic, cutaneous, articular (CINCA) syndrome and Muckle-Wells syndrome (MWS), in an effort to understand the molecular mechanisms linking mutations of the CIAS1 gene and IL-1beta hypersecretion, and the underlying response to IL-1 receptor antagonist (IL-1Ra). METHODS: Six patients with CINCA syndrome or MWS were treated with IL-1Ra and followed up longitudinally. Monocytes obtained from the patients and from 24 healthy donors were activated with lipopolysaccharide (LPS) for 3 hours, and intracellular and secreted IL-1beta levels were determined by Western blotting and enzyme-linked immunosorbent assay before and after exposure to exogenous ATP. RESULTS: LPS-induced IL-1beta secretion was markedly increased in monocytes from patients with CIAS1 mutations. However, unlike in healthy subjects, secretion of IL-1beta was not induced by exogenous ATP. Treatment with IL-1Ra resulted in a dramatic clinical improvement, which was paralleled by an early and strong down-regulation of LPS-induced IL-1beta secretion by the patients' cells in vitro. CONCLUSION: Our results showed that the requirements of ATP stimulation for IL-1beta release observed in healthy individuals are bypassed in patients bearing CIAS1 mutations. This indicates that cryopyrin is the direct target of ATP and that the mutations release the protein from the requirement of ATP for activation. In addition, the dramatic amelioration induced by IL-1Ra treatment is at least partly due to the strong decrease in IL-1beta secretion that follows the first injections of the antagonist.

These findings may have implications for other chronic inflammatory conditions characterized by increased IL-1beta.

L5 ANSWER 10 OF 124 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1253717 CAPLUS
DOCUMENT NUMBER: 148:424109
TITLE: Mutations in cryopyrin: bypassing roadblocks in the caspase 1 inflammasome for interleukin-1β secretion and disease activity
AUTHOR(S): Dinarello, Charles A.
CORPORATE SOURCE: University of Colorado Health Sciences Center, Denver, USA
SOURCE: Arthritis & Rheumatism (2007), 56(9), 2817-2822
CODEN: ARHEAW; ISSN: 0004-3591
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The research of Gattorno et al. (2007) entitled "Pattern of interleukin-1β secretion in response to lipopolysaccharide and ATP before and after interleukin-1 blockade in patients with CIAS1 mutations" is reviewed with commentary and refs. The authors studied the secretion of interleukin-1β (IL-1β) from primary blood monocytes obtained from patients with chronic infantile neurol., cutaneous, articular (CINCA) syndrome (known in North America as neonatal-onset multisystem inflammatory disease [NOMID]) and from a patient with Muckle-Wells syndrome (MWS) before and during treatment with anakinra, a recombinant human IL-1 receptor antagonist (IL-1Ra). The study focused on the function of the IL-1β "inflammasome"and the effect of mutations in cryopyrin, the protein of the NALP3 gene. The results of this study show that in vivo therapy with anakinra in patients with CIAS1 mutations was associated with an in vitro reduction in the secretion of IL-1β from monocytes as compared with secretion before treatment. Monocytes from the patient without mutations, although secreting more IL-1β than those from controls, secreted the same amount of IL-1β before, as well as after, anakinra treatment.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> display ibib abs l5 120-124
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' - CONTINUE?
(Y)/N:y

L5 ANSWER 120 OF 124 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:48026 BIOSIS
DOCUMENT NUMBER: PREV199497061026
TITLE: Effects of peripheral IL-1RA treatment after focal cerebral ischaemia in the rat.
AUTHOR(S): Relton, J. K.; Martin, D.; Russell, D.
CORPORATE SOURCE: Preclin. Pharmacol., Synergen, 1885 33rd St., Boulder, CO 80301, USA
SOURCE: Society for Neuroscience Abstracts, (1993) Vol. 19, No. 1-3, pp. 1642.
Meeting Info.: 23rd Annual Meeting of the Society for Neuroscience. Washington, D.C., USA. November 7-12, 1993.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Feb 1994
Last Updated on STN: 3 Feb 1994

L5 ANSWER 121 OF 124 MEDLINE on STN DUPLICATE 60
ACCESSION NUMBER: 1993345409 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8344218
TITLE: Endotoxin-induced corticotropin-releasing hormone gene expression in the hypothalamic paraventricular nucleus is mediated centrally by interleukin-1.
AUTHOR: Kakucska I; Qi Y; Clark B D; Lechan R M
CORPORATE SOURCE: Department of Medicine, New England Medical Center Hospitals, Boston, Massachusetts 02111.
CONTRACT NUMBER: DK-37021 (United States NIDDK)
SOURCE: Endocrinology, (1993 Aug) Vol. 133, No. 2, pp. 815-21.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 24 Sep 1993
Last Updated on STN: 24 Sep 1993
Entered Medline: 3 Sep 1993
AB In the acute phase of bacterial infection, a variety of cytokines, including interleukin-1 (IL-1), are elicited by bacterial endotoxin in both the periphery and the central nervous system. Bacterial endotoxin has been previously reported to profoundly activate the hypothalamic-pituitary-adrenal axis, resulting in elevated glucocorticoid secretion that may serve an important role as part of the inhibitory feedback mechanisms on the activated immune system. To determine whether IL-1 acts within the brain to mediate endotoxin-induced CRH gene expression in the hypothalamic paraventricular nucleus (PVN), we studied the effect of administering the human IL-1 receptor antagonist (IL-1ra) into the brain, a competitive inhibitor of IL-1, on CRH gene expression in the PVN after systemic lipopolysaccharide (LPS) treatment. Eight hours after the ip administration of LPS, the paraventricular CRH mRNA content was elevated 3-to 4-fold ($P < 0.01$) compared to the control value, and this elevation could be completely abolished by central IL-1ra pretreatment ($P < 0.05$ compared to LPS-treated group; $P > 0.05$ compared to controls). In contrast, systemic IL-1ra administration did not

inhibit endotoxin-induced CRH gene expression in the PVN. These studies demonstrate that LPS stimulates hypothalamic CRH by a mechanism that involves the action of IL-1 within the central nervous system and may proceed independently of peripheral actions of IL-1 circulating in the bloodstream.

L5 ANSWER 122 OF 124 MEDLINE on STN DUPLICATE 61
ACCESSION NUMBER: 1994073717 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8252403
TITLE: Induction of tumor necrosis factor-alpha mRNA in the brain after peripheral endotoxin treatment : comparison with interleukin-1 family and interleukin-6.
AUTHOR: Gatti S; Bartfai T
CORPORATE SOURCE: Neurochemistry and Neurotoxicology Department, Stockholm University, Sweden.
SOURCE: Brain research, (1993 Oct 8) Vol. 624, No. 1-2, pp. 291-4. Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 3 Feb 1994 Last Updated on STN: 3 Feb 1994 Entered Medline: 13 Jan 1994
AB The constitutive expression of tumor necrosis factor-alpha (TNF alpha) mRNA and its induction (60 min later) by peripheral injection of Escherichia coli lipopolysaccharide (2 mg/kg i.p.) was demonstrated by polymerase chain reaction (PCR), in the pituitary and hypothalamus but not in the striatum or hippocampus of the rat. The pattern of TNF alpha mRNA induction is different from that observed for mRNAs of IL-1 alpha and IL-1 beta, IL-1ra and IL-6 respectively. This demonstration of the induction of TNF alpha in the brain may contribute to our understanding of the central effects of TNF alpha in fever and anorexia.

L5 ANSWER 123 OF 124 MEDLINE on STN DUPLICATE 62
ACCESSION NUMBER: 1993342631 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8342131
TITLE: Interleukin-1 receptor antagonist improves survival and preserves organ adenosine-5'-triphosphate after hemorrhagic shock.
AUTHOR: Pellicane J V; DeMaria E J; Abd-Elfattah A; Reines H D; Vannice J L; Carson K W
CORPORATE SOURCE: Department of Surgery, Medical College of Virginia/Virginia Commonwealth University, Richmond 23298-0475.
SOURCE: Surgery, (1993 Aug) Vol. 114, No. 2, pp. 278-83; discussion 283-4. Journal code: 0417347. ISSN: 0039-6060.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 17 Sep 1993 Last Updated on STN: 3 Feb 1997 Entered Medline: 31 Aug 1993
AB BACKGROUND. This study was designed to determine the role of interleukin-1 (IL-1) in hemorrhagic shock death. METHODS. Pentobarbital

anesthetized C3H/HeN mice (n = 59) were prepared with a femoral arterial catheter and were randomized to treatment with an IL-1 receptor antagonist (IL-1ra, 10 mg/kg, n = 29) or an equal volume of phosphate-buffered saline solution (vehicle, n = 30) by subcutaneous bolus injection at 15 minutes before hemorrhage and again at 120 minutes. Continuous posthemorrhage delivery of IL-1ra or vehicle was performed in each group (1.5 mg IL-1ra in 30 microliters/day) through a subcutaneous osmotic pump. Rapid hemorrhage of 4 ml/100 gm weight was followed by normal saline resuscitation of 12 ml/100 gm 60 minutes later. RESULTS. Survival analysis by Wilcoxon rank sum analysis revealed a significantly improved 5-day survival in IL-1ra-treated mice (n = 15, 20%) as compared with vehicle-treated mice (n = 14, 6%, p < 0.001). To determine a possible mechanism of this survival advantage, the remaining mice in each treatment group were killed at 30 minutes to obtain blood and tissue samples from the heart, liver, and kidney for measurement of adenosine-5'-triphosphate (ATP). No difference in hematocrit, circulating neutrophils, or levels of glucose, lactate, or tumor necrosis factor was identified between groups to explain the improved outcome. IL-1ra prevented hemorrhage-induced ATP depletion observed in vital organs of vehicle-treated mice. CONCLUSIONS. The data implicate IL-1 in shock-induced ATP depletion and suggest IL-1ra may improve hemorrhagic shock survival by preventing ATP depletion in vital organs.

L5 ANSWER 124 OF 124 MEDLINE on STN DUPLICATE 63
ACCESSION NUMBER: 1992404945 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1388088
TITLE: Interleukin-1 receptor antagonist inhibits ischaemic and excitotoxic neuronal damage in the rat.
AUTHOR: Relton J K; Rothwell N J
CORPORATE SOURCE: Department of Physiological Sciences, University of Manchester, UK.
SOURCE: Brain research bulletin, (1992 Aug) Vol. 29, No. 2, pp. 243-6.
Journal code: 7605818. ISSN: 0361-9230.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 6 Nov 1992
Last Updated on STN: 3 Mar 2000
Entered Medline: 22 Oct 1992
AB Interleukin-1 (IL-1) synthesis in the brain is stimulated by mechanical injury and IL-1 mimics some effects of injury, such as gliosis and neovascularization. We report that neuronal death resulting from focal cerebral ischaemia (middle cerebral artery occlusion, 24 h) is significantly inhibited (by 50%) in rats injected with a recombinant IL-1 receptor antagonist (IL-1ra, 10 micrograms, icv 30 min before and 10 min after ischaemia). Excitotoxic damage due to striatal infusion of an NMDA-receptor agonist (cis-2,4-methanoglutamate) was also markedly inhibited (71%) by injection of the IL-1ra. These data indicate that endogenous IL-1 is a mediator of ischaemic and excitotoxic brain damage, and that inhibitors of IL-1 action may be of therapeutic value in the treatment of acute or chronic neuronal death.

=> display ibib abs l5 110-119
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' - CONTINUE?
(Y)/N:y

L5 ANSWER 110 OF 124 MEDLINE on STN DUPLICATE 54
ACCESSION NUMBER: 1996233818 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9011765
TITLE: Adrenalectomy enhances pro-inflammatory cytokines gene expression, in the spleen, pituitary and brain of mice in response to lipopolysaccharide.
AUTHOR: Goujon E; Parnet P; Laye S; Combe C; Dantzer R
CORPORATE SOURCE: INRA-INSERM U394, Bordeaux, France.
SOURCE: Brain research. Molecular brain research, (1996 Feb) Vol. 36, No. 1, pp. 53-62.
Journal code: 8908640. ISSN: 0169-328X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19 Feb 1997
Last Updated on STN: 19 Feb 1997
Entered Medline: 6 Feb 1997

AB To assess the possible influence of endogenous glucocorticoids on cytokine expression in the brain, adrenalectomized mice and sham operated mice were injected with saline or lipopolysaccharide (LPS, 10 micrograms/mouse, subcutaneously) and the levels of transcripts for IL-1 alpha, IL-1 beta, IL-1ra, IL-6 and tumor necrosis factor-alpha (TNF alpha) were determined 2 h after treatment in the spleen, pituitary, hypothalamus, hippocampus and striatum, using semi-quantitative reverse transcription polymerase chain reaction (RT-PCR). Levels of IL-1 beta were measured by ELISA in plasma and tissues of mice sacrificed after the administration of LPS or saline. LPS induced the expression of pro-inflammatory cytokines at the mRNA level in all tissues under investigation, except for TNF alpha in the hippocampus. This effect was potentiated by adrenalectomy in the spleen for IL-1 alpha and IL-1ra, the pituitary for cytokines other than IL-1ra, the hypothalamus for all cytokines, the hippocampus for cytokines other than TNF alpha, and the striatum for IL-1 alpha and IL-6. In saline-treated mice, adrenalectomy increased IL-1 alpha and IL-1 beta gene expression in the hypothalamus and IL-1 alpha gene expression in the hippocampus and striatum. LPS increased plasma and tissue levels of IL-1 beta, as determined by ELISA, and this effect was potentiated by adrenalectomy in plasma and tissues other than the spleen. These results can be interpreted to suggest that endogenous glucocorticoids regulate the neural components of the host response to infection and inflammation by inhibiting cytokine expression in peripheral organs and the brain.

L5 ANSWER 111 OF 124 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:428209 BIOSIS
DOCUMENT NUMBER: PREV199699159265
TITLE: Lower plasma CC16, a natural anti-inflammatory protein, and increased plasma interleukin-1 receptor antagonist in schizophrenia: Effects of antipsychotic drugs.
AUTHOR(S): Maes, Michael [Reprint author]; Bosmans, Eugene; Ranjan, Rakesh; Vandoolaeghe, Eric; Meltzer, Herbert Y.; De Ley, Marc; Berghmans, Raf; Stans, Greet; Desnyder, Roger
CORPORATE SOURCE: Dep. Psychiatry, Case Western Reserve Univ., Cleveland, OH, USA

SOURCE: Schizophrenia Research, (1996) Vol. 21, No. 1, pp. 39-50.
ISSN: 0920-9964.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Sep 1996
Last Updated on STN: 26 Sep 1996

AB Recently, it was suggested that in vivo activation of the monocytic and T-lymphocytic arms of cell-mediated immunity (CMI) may occur in schizophrenia and that antipsychotic drugs may modify CMI. The aim of the present study was to examine plasma soluble interleukin-2 receptor (sIL-2R), soluble suppressor/cytotoxic antigen (sCD8), interleukin-1 receptor antagonist (IL-1RA), and Clara cell protein (CC16) concentrations in normal controls, nonmedicated schizophrenic patients, and schizophrenic patients treated with risperidone or loxapine. Plasma concentrations of IL-1RA were significantly higher in nonmedicated schizophrenic patients than in normal controls. Plasma CC16 was significantly lower in nonmedicated and loxapine-treated schizophrenic patients than in normal controls, whereas risperidone-treated patients had plasma CC16 levels which were not significantly different from normal controls. Plasma CC16 levels were significantly and positively related to age at onset of schizophrenia. Plasma sIL-2R was significantly higher in schizophrenic patients who were treated with risperidone than in normal controls and nonmedicated schizophrenic patients. The results show that (i) schizophrenia is accompanied by an activation of the monocytic arm of CMI (i.e., increased plasma IL-1RA) and lower plasma levels of a natural anti-inflammatory and immunosuppressive agent, i.e. CC16, and that the latter may constitute a trait marker of schizophrenia; and that (ii) chronic treatment with atypical antipsychotic agents, i.e., risperidone, may normalize lower plasma CC16 and increase plasma sIL-2R.

L5 ANSWER 112 OF 124 EMBASE DUPLICATE 55
ACCESSION NUMBER: 1996026732 EMBASE
TITLE: Interleukin-1β (IL-β) and tumour necrosis factor (TNF) inhibit long-term potentiation in the rat dentate gyrus in vitro.
AUTHOR: Cunningham, A.J.; Murray, C.A.; O'Neill, L.A.J.; Lynch, M.A.; O'Connor, J.J. (correspondence)
CORPORATE SOURCE: Dept. Human Anatomy and Physiology, University College, Earlsfort Terrace, Dublin 2, Ireland.
SOURCE: Neuroscience Letters, (1996) Vol. 203, No. 1, pp. 17-20.
ISSN: 0304-3940 CODEN: NELED5
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Feb 1996
Last Updated on STN: 12 Feb 1996

AB The effects of the cytokine, interleukin-1β (IL-1β), and its receptor antagonist IL-1ra, were studied on long-term potentiation in the dentate gyrus of rat hippocampal slices. Field excitatory postsynaptic potentials were recorded extracellularly in the molecular region of the dentate gyrus in response to stimulation of the medial perforant path. Low frequency synaptic transmission was unaffected by IL-1β (1 ng/ml), but pre- treatment with IL-1β completely blocked induction of long-term potentiation. Co-application of IL-1β and IL-1ra (100 ng/ml) attenuated the inhibitory effect of IL-1β. In parallel with these findings, we demonstrate that IL-1β also inhibited (45)Ca influx into the slices.

The inhibitory effect of IL-1β on induction was mimicked by tumour necrosis factor (TNF; 4.5 ng/ml) and lipopolysaccharide (LPS; 10 μg/ml). These results indicate a modulatory role for cytokines in hippocampus and suggest that the inhibitory effect of IL-1β on long-term potentiation may relate to its inhibitory effect on calcium channel activity.

L5 ANSWER 113 OF 124 MEDLINE on STN
ACCESSION NUMBER: 1996356147 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8748251
TITLE: Relationship between interleukin-1 and cancer anorexia.
AUTHOR: Laviano A; Renvyle T; Meguid M M; Yang Z J; Cangiano C; Rossi Fanelli F
CORPORATE SOURCE: Department of Surgery, University Hospital SUNY Health Science Center, Syracuse 13210, USA.
CONTRACT NUMBER: DK 43796 (United States NIDDK)
SOURCE: Nutrition (Burbank, Los Angeles County, Calif.), (1995 Sep-Oct) Vol. 11, No. 5 Suppl, pp. 680-3.
Journal code: 8802712. ISSN: 0899-9007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 6 Nov 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 23 Oct 1996
AB Interleukin-1 (IL-1) induces anorexia via direct action in the brain, and its participation in the pathogenesis of cancer-associated anorexia has been hypothesized. Because the functional ablation of the ventromedial nucleus of hypothalamus (VMH), where IL-1 receptors have been detected, reverses cancer-associated anorexia in tumor-bearing (TB) rats, we hypothesize that cancer anorexia involves the direct effect of IL-1 on the VMH. To test this hypothesis, we investigated whether the intra-VMH injection of the IL-1 receptor antagonist (IL-1ra) improves food intake in anorectic TB rats. Sixteen Fischer rats (approximately 300 g/BW) were injected s.c. with 10(6) trypan-blue viable methylcholanthrene sarcoma cells, and then individually caged. Chow and water were freely available, and food intake was recorded throughout the study. Normal food intake was measured in 8 more rats, injected s.c. with normal saline. Tumor developed in all rats. When TB rats became anorectic, they were randomly assigned to either treatment or control groups. Using stereotaxic techniques, 25 ng of IL-1ra dissolved in normal saline (TB-IL-1ra; n = 8), or an equal volume of normal saline (TB-NS; n = 8) was injected bilaterally into the VMH. After surgery, rats were caged and changes in food intake recorded. At study's end, rats were sacrificed and brains removed for histological confirmation of injection sites. In the TB-NS group, food intake decreased with the occurrence of anorexia. In contrast, the intra-VMH injection of IL-1ra reduced the severity of cancer anorexia, significantly improving food intake in TB-IL-1ra rats. Data indicate that centrally acting IL-1 plays a significant role in the development of cancer anorexia.

L5 ANSWER 114 OF 124 MEDLINE on STN DUPLICATE 56
ACCESSION NUMBER: 1995310394 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7790404
TITLE: Attenuation of stroke size in rats using an adenoviral vector to induce overexpression of interleukin-1 receptor antagonist in brain.

AUTHOR: Betz A L; Yang G Y; Davidson B L
CORPORATE SOURCE: Department of Pediatrics, University of Michigan, Ann Arbor 48109-0532, USA.
CONTRACT NUMBER: NS-23870 (United States NINDS)
SOURCE: Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism, (1995 Jul) Vol. 15, No. 4, pp. 547-51. Journal code: 8112566. ISSN: 0271-678X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199507
ENTRY DATE: Entered STN: 7 Aug 1995
Last Updated on STN: 7 Aug 1995
Entered Medline: 27 Jul 1995

AB Adenoviruses have been proposed as potential vectors for gene therapy in the central nervous system, but there are no reports of their use in the treatment of a brain disease. Because central administration of interleukin-1 receptor antagonist protein (IL-1ra) reduces ischemic brain damage, we determined whether a recombinant adenovirus vector carrying the human IL-1ra cDNA (Ad.RSVIL-1ra) could be used to ameliorate brain injury in permanent focal ischemia. Groups of six rats received intraventricular injections of Ad.RSVIL-1ra or a control adenovirus containing the Escherichia coli beta-galactosidase gene (Ad.RSVlacZ). Histochemical staining for beta-galactosidase 5 days after virus injection indicated that transgene expression was confined primarily to the cells lining the ventricle. The concentrations of IL-1ra injected animals, achieving levels of 9.1 +/- 3.3 ng/g in brain and 23.7 +/- 22.5 ng/ml in CSF. In these animals, cerebral infarct volume resulting from 24 h of permanent middle cerebral artery occlusion was reduced 64%. These studies demonstrate that adenoviral vectors can be used to deliver genes that attenuate brain injury.

L5 ANSWER 115 OF 124 MEDLINE on STN DUPLICATE 57
ACCESSION NUMBER: 1996120539 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8556346
TITLE: Intracerebroventricular interleukin-1 receptor antagonist blocks the enhancement of fear conditioning and interference with escape produced by inescapable shock.
AUTHOR: Maier S F; Watkins L R
CORPORATE SOURCE: Neuroscience & Behavior Program, University of Colorado, Boulder 80309-0345, USA.
CONTRACT NUMBER: MH 00314 (United States NIMH)
MH45045 (United States NIMH)
MH50479 (United States NIMH)
SOURCE: Brain research, (1995 Oct 16) Vol. 695, No. 2, pp. 279-82. Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 12 Mar 1996
Last Updated on STN: 12 Mar 1996
Entered Medline: 27 Feb 1996

AB Brain interleukin-1 (IL-1) plays a key role in mediating the neural, endocrine, and behavioral consequences of injury and infection.

Recent evidence indicates that brain IL-1 may also be important in producing endocrine and neurochemical responses to stressors. The present experiment sought to determine whether intracerebroventricular (i.c.v.) administration of an interleukin-1 receptor antagonist (IL-1ra) would block behavioral effects of a stressor. I.c.v. application of hrIL-1ra before inescapable shock blocked the subsequent interference with escape learning and enhancement of fear conditioning normally produced by this treatment.

L5 ANSWER 116 OF 124 MEDLINE on STN DUPLICATE 58
ACCESSION NUMBER: 1996078282 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7476020
TITLE: Expression of interleukin 1 alpha, interleukin 1 beta and interleukin 1 receptor antagonist mRNA in mouse brain: regulation by bacterial lipopolysaccharide (LPS) treatment.
AUTHOR: Gabellec M M; Griffais R; Fillion G; Haour F
CORPORATE SOURCE: Unite de Pharmacologie Neuro-Immuno-Endocrinienne, Paris, France.
SOURCE: Brain research. Molecular brain research, (1995 Jul) Vol. 31, No. 1-2, pp. 122-30.
Journal code: 8908640. ISSN: 0169-328X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 24 Jan 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 7 Dec 1995
AB Lipopolysaccharide (LPS) stimulation is known to induce interleukin-1 (IL-1) mRNA expression in various immune cell types. Since IL-1 synthesis has been suggested to occur locally in brain tissue, we investigated the expression of IL-1 (alpha and beta) and IL-1 receptor antagonist (IL-1ra) mRNAs in various structures of the central nervous system, as well as in the spleen, following intraperitoneal injection of LPS (100 micrograms/mouse). After RNA extraction and amplification by the reverse transcription-polymerase chain reaction (RT-PCR), the PCR products were separated on an agarose gel, transferred and hybridized with digoxigenin-labeled probes synthetized by nested PCR. Glyceraldehyde phosphate deshydrogenase mRNA was used as an internal control. Under basal conditions the expression of IL-1 alpha, IL-1 beta and IL-1ra mRNAs in the brain was extremely low for the three cytokines; in the spleen these mRNAs were clearly detectable. Following LPS stimulation, mRNAs were strongly increased in all the tested tissues (cortex, hippocampus, hypothalamus, cerebellum, pituitary and spleen). The kinetics of mRNAs expressions in the brain were similar for all the tested regions, with a maximum at 6 h and a decrease up to 24 h after LPS administration. In the spleen the maximum was observed as soon as 1 h following stimulation. In conclusion, peripheral LPS stimulation induces a strong and transient expression of IL-1 alpha and IL-1 beta mRNAs in the brain. IL-1ra mRNA is also stimulated by LPS in various regions of the brain.(ABSTRACT TRUNCATED AT 250 WORDS)

L5 ANSWER 117 OF 124 EMBASE
ACCESSION NUMBER: 1995256395 EMBASE
TITLE: Brain interleukin-1 is involved in generation of the serum suppressive factor induced by restraint stress in mice.
AUTHOR: Zuo, Y.C.; Li, Y.F.; Mei, L.; Fan, S.G.; Ding, G.F., Prof.

(correspondence)
CORPORATE SOURCE: Department of Immunology, Beijing Medical University, 38 Xue Yuan Road, Beijing 100083, China.
SOURCE: NeuroImmunoModulation, (1995) Vol. 2, No. 2, pp. 82-87. ISSN: 1021-7401 CODEN: NROIEM
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Sep 1995
Last Updated on STN: 19 Sep 1995

AB Our previous work showed that a factor (a protein with a high molecular weight) in serum was induced by restraint stress in mice and rats, and suppressed lymphocyte proliferation induced by concanavalin A. It was also found that the generation of the serum suppressive factor was under the control of the central nervous system. The present work was designed to investigate the role of interleukin-1 (IL-1) in the brain in the generation of the serum suppressive factor. IL-1 receptor antagonist (IL-1ra) was injected intracerebroventricularly in mice and the generation of the serum suppressive factor was found to be significantly decreased in a dose-dependent manner. When the dose of IL-1ra reached 5 μg, the generation of the suppressive factor was almost totally abolished. Intracerebroventricular injection of IL-1β (1.0 pg) enhanced the generation of the suppresive factor. Taken together, these results indicate the involvement of IL-1 in the brain in mediating generation of the suppressive factor.

L5 ANSWER 118 OF 124 MEDLINE on STN
ACCESSION NUMBER: 1995104039 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7805520
TITLE: Protective effect of interleukin-1 receptor antagonist on oleic acid-induced lung injury.
AUTHOR: Zhao M W; Sun D J; Ma D L
CORPORATE SOURCE: Department of Respiratory Disease, 3rd Hospital, Beijing Medical University.
SOURCE: Zhonghua nei ke za zhi [Chinese journal of internal medicine], (1994 Mar) Vol. 33, No. 3, pp. 158-61. Journal code: 16210490R. ISSN: 0578-1426.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 15 Feb 1995
Last Updated on STN: 15 Feb 1995
Entered Medline: 27 Jan 1995

AB Thirty-six mice were divided into a control group, lung injury group by oleic acid and protected group with interleukin-1 receptor antagonist (IL-1ra). There were 12 mice in each group. Oleic acid was injected into the tail vein of the mouse with a dose of 0.2 ml/kg to produce a model of acute lung injury (ALI). The result indicates that preadministration of IL-1ra to the mouse with ALI can decrease the lung index, lung wet-to-dry weight ratio and leakage of protein from pulmonary capillary, elevate PaO2, and significantly attenuate lung histologic injury (alveoli edema, alveoli hemorrhage, lung necrosis, inflammatory cell invasion). It is suggested that IL-1ra has protective effect on oleic acid-induced lung injury and may be a potential tool for treatment of ARDS.

L5 ANSWER 119 OF 124 MEDLINE on STN DUPLICATE 59
ACCESSION NUMBER: 1994109244 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8281850
TITLE: Interleukin-1 receptor antagonist does not prevent endotoxin-induced inhibition of gastric acid secretion in rats.
AUTHOR: Saperas E; Tache Y
CORPORATE SOURCE: CURE/Digestive Disease Center, VA Wadsworth Medical Center, Los Angeles, California 90073.
CONTRACT NUMBER: DK-30110 (United States NIDDK)
MH-00663 (United States NIMH)
SOURCE: Digestive diseases and sciences, (1994 Jan) Vol. 39, No. 1, pp. 152-6.
Journal code: 7902782. ISSN: 0163-2116.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 28 Feb 1994
Last Updated on STN: 28 Feb 1994
Entered Medline: 17 Feb 1994
AB The underlying mechanisms involved in endotoxin-induced inhibition of gastric acid secretion were investigated in conscious rats with pylorus ligation for 2 hr. Intraperitoneal injection of endotoxin (0.1, 1, and 5 micrograms/rat) inhibited gastric acid output by 31%, 80%, and 84% respectively. Intraperitoneal endotoxin (1 microgram/rat) -induced inhibition of gastric acid secretion was not altered by pretreatment with the interleukin-1 receptor antagonist, IL-1RA, indomethacin, naloxone, or capsaicin. Treatments were injected peripherally at doses previously shown to antagonize the antisecretory effect of exogenous interleukin-1 beta, to inhibit prostaglandin synthesis in the stomach and brain, to block opiate receptors, and to alter functioning of unmyelinated afferent nerve fibers. These results indicate that the antisecretory effect of endotoxin can be expressed by factors other than interleukin-1, prostaglandins, or opioid peptides that do not require the integrity of capsaicin-sensitive afferent pathways.

=> display ibib abs l5 100-109
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' - CONTINUE?
(Y)/N:y

L5 ANSWER 100 OF 124 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN DUPLICATE 50
ACCESSION NUMBER: 1998322992 EMBASE
TITLE: Specificity of interleukin-1β-induced changes in monoamine concentrations in hypothalamic nuclei: Blockade by interleukin-1 receptor antagonist.
AUTHOR: Mohankumar, Sheba M.J., Dr. (correspondence); Mohankumar, P.S.; Quadri, S.K.
CORPORATE SOURCE: Neuroendocrine Research Laboratory, Kansas State University, Manhattan, KS, United States. beagle@ksu.edu
AUTHOR: Mohankumar, Sheba M.J., Dr. (correspondence)
CORPORATE SOURCE: Neuroendocrine Research Laboratory, Department of Anatomy and Physiology, VMT 102 Coll. of Vet. Medicine Sci.,

Manhattan, KS 66506, United States. beagle@ksu.edu
SOURCE: Brain Research Bulletin, (1 Sep 1998) Vol. 47, No. 1, pp. 29-34.
Refs: 40
ISSN: 0361-9230 CODEN: BRBUDU
PUBLISHER IDENT.: S 0361-9230(98)00037-9
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
026 Immunology, Serology and Transplantation
029 Clinical and Experimental Biochemistry
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Nov 1998
Last Updated on STN: 12 Nov 1998

AB The purpose of this study was to examine specificity in the effects of interleukin-1β (IL-1β) on monoamines in various areas of the hypothalamus. Adult male rats were injected i.p. with saline or 2.5 or 5.0 μg of IL-1β or were pretreated with 500 μg of IL-1 receptor antagonist (IL-1ra) followed 5 min later by 5 μg of IL-1β. The paraventricular nucleus (PVN), arcuate nucleus (AN), median eminence (ME), and medial preoptic area (MPA) were microdissected and analyzed for neurotransmitter concentrations by high- performance liquid chromatography with electrochemical detection (HPLC-EC). In the PVN, IL treatment produced significant increases in the concentrations of norepinephrine (NE), dopamine (DA), DA metabolite dihydroxyphenylacetic acid (DOPAC), serotonin (5-HT), and its metabolite 5-hydroxyindoleacetic acid (5-HIAA). IL-1 treatment increased the concentrations of NE and DA in the AN but only of NE in the ME, and it was without any effect in the MPA. Pretreatment with IL-1ra completely blocked the IL-1 effects. It is concluded that IL-1 induces highly specific changes in monoamine metabolism in the hypothalamus, and the nature of these changes depends on specific hypothalamic nuclei.

L5 ANSWER 101 OF 124 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:69017 BIOSIS
DOCUMENT NUMBER: PREV199800069017
TITLE: Inflammatory gene expression in cerebral ischemia and trauma: Potential new therapeutic targets.
AUTHOR(S): Feuerstein, Giora Z. [Reprint author]; Wang, Xinkang; Barone, Frank C.
CORPORATE SOURCE: Dep. Cardiovascular Pharmacol., SmithKline Beecham Pharm., 709 Swedeland Rd., P.O. Box 1539, King of Prussia, PA 19406, USA
SOURCE: Slikker, W., Jr. [Editor]; Trembly, B. [Editor]. Ann. N. Y. Acad. Sci., (1997) pp. 179-193. Annals of the New York Academy of Sciences; Neuroprotective agents. print.
Publisher: New York Academy of Sciences, 2 East 63rd Street, New York, New York 10021, USA. Series: Annals of the New York Academy of Sciences.
Meeting Info.: Third International Conference on Neuroprotective Agents: Clinical and Experimental Aspects. Lake Como, Italy. September 9-12, 1996. New York Academy of Sciences.
CODEN: ANYAA9. ISSN: 0077-8923. ISBN: 1-57331-092-1 (cloth), 1-57331-093-X (paper).
DOCUMENT TYPE: Book
Conference; (Meeting)
Book; (Book Chapter)

Conference; (Meeting Paper)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 1998
Last Updated on STN: 30 Jan 1998

L5 ANSWER 102 OF 124 MEDLINE on STN DUPLICATE 51
ACCESSION NUMBER: 1997296595 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9152064
TITLE: Blood serum interleukin-1 receptor antagonist in pars planitis and ocular Behcet disease.
AUTHOR: Benezra D; Maftzir G; Barak V
CORPORATE SOURCE: Immuno-Ophthalmology Unit, Hadassah University Hospital and Medical School, Jerusalem, Israel.
SOURCE: American journal of ophthalmology, (1997 May) Vol. 123, No. 5, pp. 593-8.
Journal code: 0370500. ISSN: 0002-9394.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 9 Jun 1997
Last Updated on STN: 9 Jun 1997
Entered Medline: 28 May 1997

AB PURPOSE: To determine the levels of interleukin-1 receptor antagonist (IL-1ra) in the blood serum of patients with idiopathic bilateral pars planitis and Behcet disease. METHODS: Five milliliters of blood was with-drawn from the cubital vein of 91 patients (58 with the ocular type and five with the combined type of Behcet disease; 28 with pars planitis) and 36 volunteers. Serum was separated from these samples and stored at -70 C until assayed. Interleukin-1 receptor antagonist levels were determined by human IL-1ra enzyme-linked immunosorbent assay kits. In patients not receiving any systemic medication, one serum sample was obtained before initiating treatment and another when the patients had been under full medical treatment for 6 weeks or more. RESULTS: Pretreatment mean +/- SD serum IL-1ra levels were 320 +/- 32 pg/ml for the patients with pars planitis, 380 +/- 54 pg/ml for patients with Behcet disease, and 271 +/- 29 pg/ml for the control subjects (no statistical significance). During treatment, a mean serum level of 352 +/- 37 pg/ml was observed in patients with pars planitis (not significantly different from control subjects) and 538 +/- 79 pg/ml in patients with ocular Behcet disease (P = .0116 compared with control subjects). The greatest increase in IL-1ra levels was observed in patients with Behcet disease who received a combination of cyclosporine and corticosteroids. CONCLUSIONS: Because IL-1ra is one of the natural immunomodulating molecules, the significant increase of serum IL-1ra levels, especially after combined treatment with cyclosporine and corticosteroids, could indicate that the therapeutic effects of this regimen may be mediated through its effects on this molecule.

L5 ANSWER 103 OF 124 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:260381 CAPLUS
DOCUMENT NUMBER: 126:315564
ORIGINAL REFERENCE NO.: 126:61185a,61188a
TITLE: Neurotrophins and their receptors in nerve injury and repair
AUTHOR(S): Ebadi, M.; Bashir, R. M.; Heidrick, M. L.; Hamada, F. M.; El Refaey, H.; Hamed, A.; Helal, G.; Baxi, M. D.; Cerutis, D. R.; Lassi, N. K.

CORPORATE SOURCE: Dep. Pharmacology, Univ. Nebraska College Med., Omaha, NE, 68198-6260, USA
SOURCE: Neurochemistry International (1997), 30(4/5), 347-374
CODEN: NEUIDS; ISSN: 0197-0186
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 251 refs. Cytokines are a heterogeneous group of polypeptide mediators that have been associated with activation of numerous functions, including the immune system and inflammatory responses. The cytokine families include, but are not limited to, interleukin (IL-1α, IL-1β, IL-1ra and IL-2-IL-15), chemokines (IL-8/NAP-1, NAP-2, MIP-1α and β, MCAF/MCP-1, MGSA and RANTES), tumor necrosis factors (TNF-α and TNF-β), interferons (IFN-α, β and γ), colony stimulating factors (G-CSF, M-CSF, GM-CSF, IL-3 and some of the other ILs), growth factors (EGF, FGF, PDGF, TGFα, TGFβ and ECGF), neuropoietins (LIF, CNTF< OM and IL-6), and neurotrophins (BDNF, NGF, NT-3-NT-6 and GDNF). The neurotrophins represent a family of survival and differentiation factors that exert profound effects in the central and peripheral nervous system (PNS). The neurotrophins are currently under investigation as therapeutic agents for the treatment of neurodegenerative disorders and nerve injury either individually or in combination with other trophic factors such as ciliary neurotrophic factor (CNTF) or fibroblast growth factor (FGF). Responsiveness of neurons to a given neurotrophin is governed by the expression of two classes of cell surface receptor. For nerve growth factor (NGF), these are p75NTR (p75) and p140trk (referred to as trk or trkA), which binds both BDNF and neurotrophin (NT)-4/5, and trkC receptor, which binds only NT-3. After binding ligand, the neurotrophin-receptor complex is internalized and retrogradely transported in the axon to the soma. Both receptors undergo ligand-induced dimerization, which activates multiple signal transduction pathways. These include the ras-dependent pathway utilized by trk to mediate neurotrophin effects such as survival and differentiation. Indeed, cellular diversity in the nervous system evolves from the concerted processes of cell proliferation, differentiation, migration, survival, and synapse formation. Neural adhesion and extracellular matrix mols. have been shown to play crucial roles in axonal migration, guidance, and growth cone targeting. Proinflammatory cytokines, released by activated macrophages and monocytes during infection, can act on neural targets that control thermogenesis, behavior, and mood. In addition to induction of fever, cytokines induce other biol. functions associated with the acute phase response, including hypophagia and sleep. Cytokine production has been detected within the central nervous system as a result of brain injury, following stab wound to the brain, during viral and bacterial infections (AIDS and meningitis), and in neurodegenerative processes (multiple sclerosis and Alzheimer's disease)1. Novel cytokine therapies, such as anti-cytokine antibodies or specific receptor antagonists acting on the cytokine network may provide an optimistic feature for treatment of multiple sclerosis and other diseases in which cytokines have been implicated.

REFERENCE COUNT: 251 THERE ARE 251 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 104 OF 124 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:559736 CAPLUS
DOCUMENT NUMBER: 127:246994
ORIGINAL REFERENCE NO.: 127:48243a,48246a
TITLE: Monocyte activation and ischemic brain injury: role of tumor-necrosis factor-alpha and interleukin-1

AUTHOR(S): Siren, A. - L.; Mccarron, R.; Wang, L.; Garcia-Pinto, P.; Ruetzler, C.; Martin, D.; Felgenhauer, K.; Hallenbeck, J. M.
CORPORATE SOURCE: Department of Neurology, The Uniformed Services University of the Health Sciences, Bethesda, MD, 20814, USA
SOURCE: Pharmacology of Cerebral Ischemia 1996, [International Symposium on Pharmacology of Cerebral Ischemia], 6th, Marburg, July 21-24, 1996 (1996), 429-435. Editor(s): Krieglstein, Josef. Medpharm Scientific Publishers: Stuttgart, Germany.
CODEN: 64YHA7
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The role of monocyte activation in the development of cerebral infarcts was examined in rats subjected to a modified local Shwartzman reaction by an intracerebroventricular (i.c.v.) bolus injection of lipopolysaccharide (LPS). Two weeks after chronic monocyte activation by an i.v. injection Bacillus Calmette Guerin (BCG) spontaneous formation of superoxide anions, an indicator for leukocyte activation, was present in 94.2% of the whole blood monocytes compared to 18.1% of the monocytes after vehicle treatment. Expression of β2-integrins was increased by 1.3 to 2-fold in monocytes of BCG-treated rats. Two weeks after priming with BCG, administration of LPS (100 μg/10 μl, i.c.v) resulted in paralysis and death of over 85% of the animals. None of the saline-treated rats were vulnerable to paralysis or death after this dose of LPS. Histol. evaluation of the brains of neurol. impaired and moribund animals revealed intravascular thrombosis and pale and hemorrhagic infarcts in the forebrain. The hippocampal pyramidal cells that exhibit selective vulnerability to global ischemia were preserved in all animals. Infiltrates of leukocytes were found around blood vessels, cerebral ventricles and meninges in all LPS injected rats. Treatment (2 + 100 μg/10 μl, i.c.v.) with the polyethylene glycol-conjugated dimer of the recombinant human TNF 55kDA receptor (TNFbp) completely prevented the paralysis and deaths in this model while the recombinant human IL-1 receptor antagonist (IL-1ra, 2 + 100 μg/10 μl, i.c.v.) decreased the incidence of paralysis and death to 40%. The improvement of neurol. symptoms was accompanied with reduced histol. damage in the brain tissue. The results suggest that chronic monocyte activation predisposes stroke-risk free animals to thrombosis and hemorrhage via an exaggerated release of proinflammatory cytokines.

L5 ANSWER 105 OF 124 BIOSIS
ACCESSION NUMBER: 1996:317439 BIOSIS
DOCUMENT NUMBER: PREV199699039795
TITLE: Circulating serum levels of IL-1ra in patients with relapsing remitting multiple sclerosis are normal during permission phases but significantly increased either during exacerbations or in response to IFN-beta treatment.
AUTHOR(S): Nicoletti, Ferdinando [Reprint author]; Patti, Francesco; Di Marco, Roberto; Zaccone, Paola; Nicoletti, Alessandra; Meroni, Pier Luigi; Reggio, Arturo
CORPORATE SOURCE: via Luigi Sturzo n. 3, 95021, Cannizsaro, Catania, Italy
SOURCE: Cytokine, (1996) Vol. 8, No. 5, pp. 395-400.
CODEN: CYTIE9. ISSN: 1043-4666.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 1996
Last Updated on STN: 11 Jul 1996

AB Interleukin (IL)-1 receptor antagonist (IL-1ra) is a naturally occurring inhibitor of IL-1 which binds to IL-1 receptors without generating immunologic responses. Evidence has recently been provided that the balance between the production of IL-1 and IL-1ra might influence the course of immunoinflammatory diseases such as inflammatory bowel diseases, rheumatoid arthritis (RA) and Lyme arthritis. To assess whether endogenous IL-1ra may also have a role on the course of multiple sclerosis (MS) we presently studied the fluctuation of the serum levels of IL-1ra in patients with relapsing remitting (RR) MS either during remission or exacerbation. Moreover, to evaluate whether the beneficial effect of IFN-beta on the course of MS might also be mediated by an increased production of IL-1ra, we measured the levels of circulating IL-1ra in MS patients prior to and after 6 months of continuous treatment with natural human IFN-beta (6 000 000 IU three times a week for 6 months). Our results demonstrated that, relative to control subjects, IL-1ra serum levels are 'normal' during remitting phases of RR MS but significantly elevated either during exacerbations or in response to IFN-beta treatment.

L5 ANSWER 106 OF 124 MEDLINE on STN DUPLICATE 52
ACCESSION NUMBER: 1997055461 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8899748
TITLE: Induction of interleukin-1 beta and interleukin-1 receptor antagonist mRNA by chronic treatment with various psychotropics in widespread area of rat brain.
AUTHOR: Suzuki E; Shintani F; Kanba S; Asai M; Nakaki T
CORPORATE SOURCE: Department of Neuropsychiatry, Keio University School of Medicine, Tokyo, Japan.
SOURCE: Neuroscience letters, (1996 Sep 13) Vol. 215, No. 3, pp. 201-4.
Journal code: 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 13 Mar 1997
Last Updated on STN: 13 Mar 1997
Entered Medline: 28 Feb 1997
AB We investigated whether psychotropics orally administered to rats affect levels of interleukin-1 beta (IL-1 beta) and interleukin-1 receptor antagonist (IL-1Ra) mRNA in the hypothalamus, hippocampus, frontal cortex, and brain stem, using a reverse transcription-polymerase chain reaction method. The psychotropics tested were chlorpromazine, haloperidol, imipramine, maprotiline, fluvoxamine, and diazepam. Treatment for 28 days raised the levels of both mRNAs. The increase in IL-1Ra mRNA was 6-112 times larger than that of IL-1 beta mRNA in most brain regions examined. These results suggest that chronic treatment with psychotropics causes greater amplifying effects on IL-1Ra mRNA than IL-1 beta mRNA in the brain.

L5 ANSWER 107 OF 124 MEDLINE on STN DUPLICATE 53
ACCESSION NUMBER: 1996193026 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8622824
TITLE: Mechanisms of sickness-induced decreases in food-motivated behavior.
AUTHOR: Kent S; Bret-Dibat J L; Kelley K W; Dantzer R
CORPORATE SOURCE: Stanford University School of Medicine, Department of

Psychiatry and Behavioral Science, CA 94305-5095, USA.
SOURCE: Neuroscience and biobehavioral reviews, (1996) Vol. 20, No. 1, pp. 171-5. Ref: 36
Journal code: 7806090. ISSN: 0149-7634.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 27 Jun 1996
Last Updated on STN: 27 Jun 1996
Entered Medline: 14 Jun 1996

AB Interleukin-1 beta (IL-1 beta) is a cytokine released by activated macrophages and monocytes, which mediates many of the local and systemic responses to inflammation. Interleukin-1 beta induces anorexia in rats when administered peripherally or centrally. An endogenous antagonist for the IL-1 type I receptor has been characterized and cloned (IL-1ra). We have used this protein to ascertain the site of action for the anorexic effects of IL-1 beta. Male rats were food restricted and trained on an operant schedule for food reinforcement. Administration of recombinant human IL-1 beta (4 micrograms i.p. or 40 ng i.c.v.) induced profound decreases in operant responding, with maximal effects 1-4 h post-injection. Interleukin-1ra pretreatment (2.4 mg i.p. or 24 micrograms i.c.v.) completely blocked these effects when administered by the same route. In contrast, i.c.v. Il-1ra only partially blocked the effects of i.p. IL-1 beta, and i.p. IL-1ra was unable to block the effects of i.c.v. IL-1 beta. Interleukin-1ra did not affect responding by itself. These results suggest that IL-1 beta acts as both peripheral and central IL-1 receptors to reduce food motivated behavior. To determine the central site of action of IL-1 beta, small quantities of IL-1 beta (5 and 30 ng) were infused into the ventromedial hypothalamus of male rats. Both doses produced profound decreases in responding; the magnitude and time course of these effects were nearly identical to those observed after i.c.v. administration. These results suggest that the VMH may serve as a central site of action for the depressive effects of IL-1 beta on food intake. There is much controversy over the pathways of communication from the immune system to the brain. To test the hypothesis that the peripheral immune stimulus is transmitted to the brain via a neutral communication pathway, mice were injected with lipopolysaccharide at a behaviorally active dose (10 micrograms i.p.). This treatment increased the concentrations of substance P, neurokinin A, and calcitonin gene-related peptide in mouse spinal cord in a prostaglandin-dependent manner. Maximal increases in neuropeptide content were observed 1 h post-injection. Finally, subdiaphragmatic vagotomy was found to attenuate the reduction in food-motivated behavior induced by both IL-1 beta and lipopolysaccharide in mice.

L5 ANSWER 108 OF 124 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:178547 CAPLUS
DOCUMENT NUMBER: 124:258051
ORIGINAL REFERENCE NO.: 124:47809a,47812a
TITLE: Increased survival in experimental rat heatstroke by continuous perfusion of interleukin-1 receptor antagonist
AUTHOR(S): Chiu, W.T.; Kao, T.Y.; Lin, M.T.
CORPORATE SOURCE: Department of Public Health, Taipei Medical College, Taipei, Taiwan
SOURCE: Neuroscience Research (Shannon, Ireland) (1996),

24(2), 159-63
CODEN: NERADN; ISSN: 0168-0102
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To assess the possible therapeutic value of interleukin-1 receptor antagonist (IL-1ra) in the treatment of heatstroke, the authors evaluated the effects of heatstroke on survival time (interval between onset of heatstroke and death), systemic and striatal hemodynamic changes, and extent of striatal neuronal damage in rats treated with saline or IL-1ra. The survival time of the heatstroke rats which received normal saline (single injection or continuous perfusion) was about 17 min. The heatstroke-induced ischemic damage to striatal neurons was due to systemic arterial hypotension, intracranial hypertension, decreased cerebral perfusion, and striatal dopamine (DA) accumulation (275%). Rats treated with a single injection of IL-1ra (200 μg/kg, i.v.) immediately after the onset of heatstroke survived much longer (91 min) than the controls. The prolongation of survival induced by IL-1ra was brought about by attenuation of the arterial hypotension, intracranial hypertension, decreased cerebral perfusion, ischemic damage to striatal neurons, and striatal DA release value (204%). Furthermore, after continuous perfusion of IL-1ra (200 μg/kg per h, i.v.) immediately after the onset of heatstroke, the striatal DA release value of the rats was further reduced to 140% while the survival time of the rats was prolonged to up to 10 h from the onset of heatstroke. Thus, it appears that continuous i.v. perfusion of IL-1ra is a good choice for heatstroke therapy.

L5 ANSWER 109 OF 124 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:283927 BIOSIS
DOCUMENT NUMBER: PREV199699006283
TITLE: Clinical and immunological considerations in Epstein-Barr virus-associated diseases.
AUTHOR(S): Andersson, Jan
CORPORATE SOURCE: Dep. Infect. Dis., Karolinska Inst., Huddinge Univ. Hosp., I-63, S-141 86 Huddinge, Sweden
SOURCE: Scandinavian Journal of Infectious Diseases Supplementum, (1996) Vol. 0, No. 100, pp. 72-82.
CODEN: SJISAH. ISSN: 0300-8878.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jun 1996
Last Updated on STN: 25 Jun 1996
AB Despite the fact that nucleoside analogues, such as acyclovir and ganciclovir, and DNA-polymerase inhibitors, such as foscarnet, have a proven antiviral effect on oropharyngeal-Epstein-Barr virus (EBV) replication, they have been unable to show any effect on the severity or duration of infectious mononucleosis (IM), a condition for which there is currently no established treatment. Clinical symptoms may be due to an EBV-induced polyclonal humoral, as well as cellular, immunoreactivity with limited pathology caused by viral replication itself. However, despite an extensive immune response, 90% of tested IM patients (n = 36) had a spontaneous outgrowth of in vivo EBV-infected B-lymphocytes at onset of disease, indicating lack of specific EBV-restricted cellular cytotoxicity at this time. Establishment of an EBV-specific T-lymphocyte response occurred 90-180 days after onset of disease (human leukocyte antigen-restricted cytotoxicity against EBV-infected B-cells). Thus, development of a specific cytotoxic response was a gradual and slow process. Assessment of cytokine pattern, at the

single cell level, was performed by immunocytochemical technique and by enzyme-linked immunosorbent assay. This revealed an increased production of interleukin (IL)-2, interferon (IFN)-gamma, IL-6 and tumour necrosis factor (TNF)beta in all IM patients. Those with disseminated disease were characterized by lack of IFN-gamma production. This loss was selective since in vitro stimulation with superantigen, such as streptococcal pyrogenic exotoxin A, induced a normal response. These patients lacked signs of EBV-specific T-cell cytotoxicity in vitro. Treatment with intravenous or subcutaneous IFN-gamma, 1.5 MU every second day, in combination with intravenous immunoglobulin G (0.5 g/kg three times per week) and oral acyclovir, 800 mg 5 times daily, has shown promising results in some patients. Cytokine production in tonsil tissue in 4 patients with fulminant IM and respiratory tract obstruction showed a concomitant expression of IL-2, IFN-gamma, IL-6, TNF beta, transforming growth factor (TGF)beta-1-3, granulocyte colony stimulating factor, granulocyte macrophage colony stimulating factor, IL-4 IL-1-alpha, IL-beta, IL-1ra and TNF-alpha. The number of M-2, IFN-gamma, IL-6 and TNF-beta producing cells was significantly higher compared to tonsil tissue obtained from children with tonsillar hypertrophy. Thus, IM is associated with extensive local cytokine production. It is suggested that this extensive cytokine production is closely involved in the pathology of IM and that patients with atypical IM have a dysregulation in the cytokine network. However, the mechanism by which EBV-infected B-lymphocytes triggers this cytokine cascade is still unknown. These findings show the need for evaluation of patients with immunodeficiency and EBV-induced lymphoproliferative disorders and perhaps the introduction of new immunoregulatory treatment strategies.

=> display ibib abs l5 90-99
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' - CONTINUE?
(Y)/N:y

L5 ANSWER 90 OF 124 MEDLINE on STN
ACCESSION NUMBER: 1999217635 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10202985
TITLE: Cytokine-induced inflammation and long-term stroke functional outcome.
AUTHOR: Vila N; Filella X; Deulofeu R; Ascaso C; Abellana R; Chamorro A
CORPORATE SOURCE: Service of Neurology, Hospital Clinic i Provincial, Barcelona, Spain.
SOURCE: Journal of the neurological sciences, (1999 Jan 15) Vol. 162, No. 2, pp. 185-8.
Journal code: 0375403. ISSN: 0022-510X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 12 Jul 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 22 Jun 1999
AB Inflammatory reactions are involved in the pathogenesis of cerebral ischemia. Cytokines exacerbate brain ischemic injury by several mechanisms and they activate the synthesis of acute-phase reactants. We evaluated the association between cytokine-induced inflammation and

functional outcome in 41 patients with acute ischemic stroke. Blood samples for interleukin-1 receptor antagonist (IL-1ra), erythrocyte sedimentation rate (ESR), c-reactive protein (CRP) and polymorphonuclear leukocyte (PMNL) count were taken within 48 h from stroke onset. Functional outcome was assessed at six months with the Modified Rankin Scale. Patients with a Rankin score > or = 3 were classified as dependent outcome. The effect of inflammatory variables on outcome was analyzed by logistic regression. Mathew score <75 on admission, atrial fibrillation, non-lacunar infarct size, ESR>13 mm/h in men or >20 mm/h in women, PMNL count >8 x 10(9)/l, CRP>0.8 mg/dl and IL-1ra>500 pg/ml were associated with dependent outcome. On multiple logistic regression, severe stroke on admission, non-lacunar infarct size and ESR remain in the predictive model of outcome with a sensitivity and specificity of 76 and 80%, respectively. This study suggests that in addition to clinical evaluation and neuroimaging, measurement of ESR may be useful for the early detection of stroke patients with poor long-term functional outcome.

L5 ANSWER 91 OF 124 MEDLINE on STN DUPLICATE 43
ACCESSION NUMBER: 1999280355 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10350527
TITLE: The role of brain cytokines in mediating the behavioral and neuroendocrine effects of intracerebral mycoplasma fermentans.
AUTHOR: Yirmiya R; Weidenfeld J; Barak O; Avitsur R; Pollak Y; Gallily R; Wohlman A; Ovadia H; Ben-Hur T
CORPORATE SOURCE: Department of Psychology, The Hebrew University of Jerusalem, Mount Scopus, Jerusalem 91905, Israel.. msrazy@mscc.huji.ac.il
SOURCE: Brain research, (1999 May 22) Vol. 829, No. 1-2, pp. 28-38. Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 16 Aug 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 2 Aug 1999

AB Intracerebral administration of Mycoplasma fermentans (MF), a small microorganism that has been found in the brain of some AIDS patients, induces behavioral and neuroendocrine alterations in rats. To examine the role of tumor necrosis factor-alpha (TNFalpha) and interleukin-1 (IL-1) in mediating these effects we measured MF-induced expression of TNFalpha and IL-1beta mRNA in various brain regions, and the effects of TNFalpha synthesis blockers and IL-1 receptor antagonist (IL-1ra) on MF-induced sickness behavior and adrenocortical activation. Intracerebroventricular (i.c.v.) administration of heat-inactivated MF induced the expression of both TNFalpha and IL-1beta mRNA in the cortex, dorsal hippocampus, amygdala, and hypothalamus. Pre-treatment of rats with either TNFalpha synthesis blockers, pentoxifylline or rolipram, or with IL-1ra did not attenuate MF-induced anorexia, body weight loss, and suppression of social behavior. However, simultaneous administration of both pentoxifylline and IL-1ra markedly attenuated MF-induced anorexia and body weight loss, but had no effect on the suppression of social behavior. Pre-treatment with pentoxifylline, but not with IL-1ra, significantly attenuated MF-induced corticosterone (CS) secretion. Together, these findings indicate that both TNFalpha and IL-1 participate, in a

complementary manner, in mediating some of the behavioral effects of MF, whereas only TNFalpha, but not IL-1, is involved in mediating MF-induced adrenocortical activation. We suggest that cytokines within the brain are involved in mediating at least some of the neurobehavioral and neuroendocrine abnormalities that may be produced by MF in AIDS patients.

L5 ANSWER 92 OF 124 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:501184 CAPLUS
DOCUMENT NUMBER: 129:145626
ORIGINAL REFERENCE NO.: 129:29595a,29598a
TITLE: Interleukin-1 receptor antagonist beta (IL-1ra β)
INVENTOR(S): Young, Peter R.
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 855404	A1	19980729	EP 1998-300572	19980127
EP 855404	B1	20010613		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 5863769	A	19990126	US 1997-790032	19970128
JP 10304888	A	19981117	JP 1998-52620	19980128
JP 2000032990	A	20000202	JP 1999-134172	19980128
CA 2232812	A1	19990920	CA 1998-2232812	19980320
PRIORITY APPLN. INFO.:			US 1997-790032 A	19970128
			JP 1998-52620 A3	19980128

AB IL-1ra beta polypeptides and polynucleotides and methods for producing such polypeptides by recombinant techniques are disclosed. Also disclosed are methods for utilizing IL-1ra beta polypeptides and polynucleotides in the design of protocols for the treating chronic and acute inflammation, septicemia, cancer, anemia, arthritis, inflammatory bowel disease, graft vs. host disease, autoimmunity, stroke, cardiac ischemia, acute respiratory disease syndrome (ARDS), psoriasis, restenosis, traumatic brain injury, AIDS, cachexia, among others, and diagnostic assays for such conditions. Thus, cDNA sequences for IL-1ra β were isolated, sequenced, cloned and expressed.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 93 OF 124 MEDLINE on STN DUPLICATE 44
ACCESSION NUMBER: 1998234427 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9565638
TITLE: Production of mice deficient in genes for interleukin (IL)-1alpha, IL-1beta, IL-1alpha/beta, and IL-1 receptor antagonist shows that IL-1beta is crucial in turpentine-induced fever development and glucocorticoid secretion.
AUTHOR: Horai R; Asano M; Sudo K; Kanuka H; Suzuki M; Nishihara M; Takahashi M; Iwakura Y
CORPORATE SOURCE: Laboratory Animal Research Center, Institute of Medical Science, University of Tokyo, Minato-ku, Tokyo 108, Japan.
SOURCE: The Journal of experimental medicine, (1998 May 4) Vol.

187, No. 9, pp. 1463-75.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 11 Jun 1998
Last Updated on STN: 11 Jun 1998
Entered Medline: 4 Jun 1998

AB Interleukin (IL)-1 is a major mediator of inflammation and exerts pleiotropic effects on the neuro-immuno-endocrine system. To elucidate pathophysiological roles of IL-1, we have first produced IL-1alpha/beta doubly deficient (KO) mice together with mice deficient in either the IL-1alpha, IL-1beta, or IL-1 receptor antagonist (IL-1ra) genes. These mice were born healthy, and their growth was normal except for IL-1ra KO mice, which showed growth retardation after weaning. Fever development upon injection with turpentine was suppressed in IL-1beta as well as IL-1alpha/beta KO mice, but not in IL-1alpha KO mice, whereas IL-1ra KO mice showed an elevated response. At this time, expression of IL-1beta mRNA in the diencephalon decreased 1.5-fold in IL-1alpha KO mice, whereas expression of IL-1alpha mRNA decreased >30-fold in IL-1beta KO mice, suggesting mutual induction between IL-1alpha and IL-1beta. This mutual induction was also suggested in peritoneal macrophages stimulated with lipopolysaccharide in vitro. In IL-1beta KO mice treated with turpentine, the induction of cyclooxygenase-2 (EC 1.14.99.1) in the diencephalon was suppressed, whereas it was enhanced in IL-1ra KO mice. We also found that glucocorticoid induction 8 h after turpentine treatment was suppressed in IL-1beta but not IL-1alpha KO mice. These observations suggest that IL-1beta but not IL-1alpha is crucial in febrile and neuro-immuno-endocrine responses, and that this is because IL-1alpha expression in the brain is dependent on IL-1beta. The importance of IL-1ra both in normal physiology and under stress is also suggested.

L5 ANSWER 94 OF 124 MEDLINE on STN DUPLICATE 45
ACCESSION NUMBER: 1998365074 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9701344
TITLE: Exacerbation of ischemic brain damage by localized striatal injection of interleukin-1beta in the rat.
AUTHOR: Stroemer R P; Rothwell N J
CORPORATE SOURCE: School of Biological Sciences, University of Manchester, United Kingdom.
SOURCE: Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism, (1998 Aug) Vol. 18, No. 8, pp. 833-9.
Journal code: 8112566. ISSN: 0271-678X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 3 Sep 1998
Last Updated on STN: 3 Mar 2000
Entered Medline: 21 Aug 1998

AB Interleukin-1beta (IL-1beta) has been implicated in ischemic brain damage. The site of action of IL-1beta in such damage is not known, but we have demonstrated previously that injection of the interleukin-1

receptor antagonist (IL-1ra) in the striatum but not the cortex of rats inhibits damage caused by permanent middle cerebral artery occlusion. The present study investigated the site of action of IL-1beta on ischemic damage by examining the effects of intracerebroventricular, striatal, or cortical injection of recombinant IL-1beta at the onset of permanent middle cerebral artery occlusion in the rat. Intracerebroventricular injection of IL-1beta (2.5 ng) significantly increased infarct volume in the striatum (35%, P < 0.0001) and in the cortex (44%, P < 0.0001) compared with vehicle treatment. Direct injection of IL-1beta into the striatum also increased infarct volume in both the striatum (36%, P < 0.0001) and the cortex (38%, P < 0.0001), whereas injection of IL-1beta into the cortex failed to affect infarct volume in either the striatum or the cortex. Cortical injection of a higher dose of IL-1beta (20 ng) also failed to affect ischemic damage in either the striatum or the cortex. Injection of IL-1beta into the striatum contralateral to the infarction had no effect on striatal damage in the ischemic hemisphere, but did increase cortical damage by 18% (P < 0.0001). In separate groups of animals, IL-1beta (2.5 ng) was injected into either the striatum or the cortex, and body temperature was recorded continuously in conscious free-moving animals by remote telemetry. Injection of IL-1beta at either site failed to influence body temperature, suggesting that exacerbation of brain damage by striatal injection of IL-1beta is not caused by effects on body temperature. These results imply that IL-1beta exacerbates ischemic damage by specific actions in the striatum where it can influence damage at distant sites in the cortex.

L5 ANSWER 95 OF 124 MEDLINE on STN DUPLICATE 46
ACCESSION NUMBER: 1998283137 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9619378
TITLE: Different roles of brain interleukin 1 in the adrenocorticotropin response to central versus peripheral administration of lipopolysaccharide in the rat.
AUTHOR: Habu S; Watanobe H; Yasujima M; Suda T
CORPORATE SOURCE: Third Department of Internal Medicine, Hirosaki University School of Medicine, Aomori, Japan.
SOURCE: Cytokine, (1998 May) Vol. 10, No. 5, pp. 390-4.
Journal code: 9005353. ISSN: 1043-4666.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 28 Aug 1998
Last Updated on STN: 28 Aug 1998
Entered Medline: 17 Aug 1998

AB Although it is well established that peripheral administration of endotoxin activates the hypothalamic-pituitary-adrenal (HPA) axis, information is very limited regarding whether central administration of endotoxin can similarly stimulate the endocrine axis. Moreover, it is also unknown whether a difference exists in the mode of involvement of brain-derived cytokines in determining the HPA response to peripheral vs central administration of endotoxin. In the present study, the authors attempted to gain more knowledge on these issues focusing on interleukin (IL) 1 in the brain, one of key pro-inflammatory cytokines mediating the immuno-endocrine network. In male rats, both intravenous (i.v., 100 micrograms/kg body weight) and intracerebroventricular [i.c.v. (the 3rd ventricle), 10 micrograms] injections of Escherichia coli lipopolysaccharide (LPS) caused a significant elevation of adrenocorticotropin (ACTH) levels in plasma, even though peaked ACTH responses occurred earlier after the i.v. (60 min

post-injection) than the i.c.v. (120 min post-injection) LPS. Although the ACTH response to i.c.v. LPS was significantly suppressed by a prior (5 min) i.c.v. administration of IL-1 receptor antagonist (IL-1Ra, 1 microgram), the hormonal response to i.v. LPS was not. That this dose of IL-1Ra was not biologically a small dose was indicated by another experiment that the same dose of i.c.v. IL-1Ra was able to significantly suppress the ACTH response to an i.c.v. injection of recombinant human IL-1 beta (50 ng). These results suggest that i.c.v. LPS, as i.v. LPS, can stimulate ACTH secretion in the rat, and this hormonal response may, at least in part, be mediated by brain-derived IL-1. Although there is one previous study reporting an important role of central IL-1 in mediating the HPA response to systemic LPS treatment, our present data suggest that such a mechanism may not operate before and during an early, peak phase of ACTH secretion after i.v. LPS.

L5 ANSWER 96 OF 124 MEDLINE on STN DUPLICATE 47
ACCESSION NUMBER: 1998142684 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9481685
TITLE: Involvement of interleukin-1, prostaglandins and mast cells in rectal distension-induced colonic water secretion in rats.
AUTHOR: Eutamene H; Theodorou V; Vergnolle N; Comera C; Fioramonti J; Bueno L
CORPORATE SOURCE: Institut National de la Recherche Agronomique, Pharmacology and Toxicology Unit, Toulouse, France.
SOURCE: The Journal of physiology, (1998 Jan 1) Vol. 506 (Pt 1), pp. 245-52.
Journal code: 0266262. ISSN: 0022-3751.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 16 Apr 1998
Last Updated on STN: 16 Apr 1998
Entered Medline: 3 Apr 1998
AB 1. In vivo rectal distension (RD) induces a neurally mediated colonic net water hypersecretion in rats. Interleukin-1 beta (IL-1 beta) also induces neural colonic water hypersecretion involving the release of prostaglandins (PGs) and a mast cell degranulation in rats. This study investigated in vivo the role of IL-1, PGs and mast cells in RD-induced colonic hypersecretion. 2. Proximal colonic net water flux was determined using [14C]polyethylene glycol (PEG) 4000 (mol. weight 4000) in anaesthetized rats. On strips taken from the distal colon: (i) a histological analysis was performed to determine the number of mucosal mast cells (MMC); and (ii) histamine levels were measured by radioimmunoassay after stimulation with compound 48/80. 3. RD induced a net colonic water secretion that was blocked by i.c.v. administration of IL-1ra (an IL-1 receptor antagonist) and indomethacin, and by systemic treatment with doxantrazole and indomethacin. RD decreased the number of resident mast cells and the release of histamine from the distal colonic strips. Moreover, using SDS-PAGE immunoblotting the expression of IL-1 beta was detected in the brain. 4. These results suggest that, in rats, RD induces colonic net water hypersecretion by the activation of a neuro-immunological reflex pathway, involving IL-1 beta, PG release and peripheral mast cell degranulation.

L5 ANSWER 97 OF 124 MEDLINE on STN
ACCESSION NUMBER: 1999081453 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9865855
TITLE: Modulation of TNF-alpha mRNA production in rat C6 glioma

cells by TNF-alpha, IL-1beta, IL-6, and IFN-alpha: in vitro analysis of cytokine-cytokine interactions.
AUTHOR: Gayle D; Ilyin S E; Miele M E; Plata-Salaman C R
CORPORATE SOURCE: Division of Molecular Biology, School of Life and Health Sciences, University of Delaware, Newark 19716-2590, USA.
SOURCE: Brain research bulletin, (1998 Oct) Vol. 47, No. 3, pp. 231-5.
Journal code: 7605818. ISSN: 0361-9230.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 26 Mar 1999
Last Updated on STN: 26 Mar 1999
Entered Medline: 18 Mar 1999

AB Cytokines regulate the expression of other cytokines in the centrally derived rat C6 glioma cell line. However, the modulation of tumor necrosis factor-alpha (TNF-alpha, a pivotal proinflammatory cytokine) in C6 cells is unknown. Here we investigated the expression of TNF-alpha mRNA in C6 glioma cells in response to TNF-alpha, interleukin-1beta (IL-1beta), IL-1 receptor antagonist (IL-1Ra), interleukin-6 (IL-6), and interferon-alpha (IFN-alpha). The data show that (1) IL-1beta induced a significant upregulation of TNF-alpha mRNA; (2) the effect of IL-1beta on TNF-alpha mRNA expression was completely blocked by the concomitant application of IL-1Ra, which suggests specificity of IL-1beta action through the IL-1 signaling receptor; (3) no detectable modulation of TNF-alpha mRNA expression was observed with the individual applications of TNF-alpha, IL-6, or IFN-alpha; (4) the concomitant treatments of TNF-alpha + IL-1beta or TNF-alpha + IL-1beta + IL-6 strongly upregulated TNF-alpha mRNA expression, whereas the concomitant application of TNF-alpha + IL-6 or IL-1beta + IL-6 induced a moderate increase; and (5) IFN-alpha significantly attenuated induction of TNF-alpha mRNA by TNF-alpha + IL-1beta + IL-6. Thus, IL-1beta, TNF-alpha and IL-6 interact to upregulate TNF-alpha mRNA expression synergistically, and IFN-alpha acts as an inhibitory cytokine in C6 glioma cells. These findings also suggest that the rat C6 glioma cell line may be used as an in vitro model to characterize cytokine-cytokine interactions.

L5 ANSWER 98 OF 124 MEDLINE on STN DUPLICATE 48
ACCESSION NUMBER: 1998288166 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9622598
TITLE: Lipopolysaccharide (LPS)- and muramyl dipeptide (MDP)-induced anorexia during refeeding following acute fasting: characterization of brain cytokine and neuropeptide systems mRNAs.
AUTHOR: Gayle D; Ilyin S E; Flynn M C; Plata-Salaman C R
CORPORATE SOURCE: Division of Molecular Biology, School of Life and Health Sciences, University of Delaware, Newark, DE 19716-2590, USA.
SOURCE: Brain research, (1998 Jun 8) Vol. 795, No. 1-2, pp. 77-86.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 28 Aug 1998

Last Updated on STN: 28 Aug 1998
Entered Medline: 19 Aug 1998

AB We investigated the effectiveness of lipopolysaccharide (LPS) and muramyl dipeptide (MDP) administered into the brain to induce anorexia in acutely fasted Wistar rats allowed to refeed. We also assayed for changes in mRNA levels of IL-1 system components, TNF-alpha, TGF-beta1, glycoprotein 130 (gp 130), leptin receptor (OB-R), pro-opiomelanocortin (POMC), neuropeptide Y (NPY), glucocorticoid receptor (GR), and CRF receptor (CRF-R) in selected brain regions. The data show that LPS and MDP induced anorexia differentially during refeeding. LPS-induced anorexia was of a stronger magnitude and duration than that of MDP. RNase protection assays showed that LPS and MDP significantly increased the expression of IL-1beta, IL-1 receptor type I, and TNF-alpha mRNAs in the cerebellum, hippocampus, and hypothalamus; LPS was more potent in all cases. MDP treatment, on the other hand, induced a stronger increase in hypothalamic levels of IL-1 receptor antagonist (IL-1Ra) and TGF-beta1 mRNAs relative to LPS. In addition, competitive RT-PCR analysis showed that LPS induced an eleven-fold increase in IL-1alpha mRNA in the hypothalamus relative to vehicle. These findings suggest that LPS and MDP mediate anorexia through different cytokine mechanisms. A stronger up-regulation of anti-inflammatory cytokines (IL-1Ra and TGF-beta1) mRNA expression by MDP may be involved in the weaker MDP-induced anorexia relative to LPS. No significant changes were observed in the peptide components examined except for an up-regulation in cerebellar gp 130 mRNA and down-regulation of hypothalamic GR mRNA expression in response to LPS or MDP. This study shows that LPS and MDP induce anorexia in fasted rats allowed to refeed, and suggests an important role for endogenous cytokine-cytokine interactions.

L5 ANSWER 99 OF 124 MEDLINE on STN DUPLICATE 49
ACCESSION NUMBER: 1998090412 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9430547
TITLE: Interleukin-1 receptor antagonist suppresses Langerhans cell activity and promotes ocular immune privilege.
AUTHOR: Dana M R; Dai R; Zhu S; Yamada J; Streilein J W
CORPORATE SOURCE: Schepens Eye Research Institute, and the Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts 02114, USA.
CONTRACT NUMBER: EY00363 (United States NEI)
EY06622 (United States NEI)
EY19765 (United States NEI)
+
SOURCE: Investigative ophthalmology & visual science, (1998 Jan) Vol. 39, No. 1, pp. 70-7.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 30 Jan 1998
Last Updated on STN: 30 Jan 1998
Entered Medline: 21 Jan 1998

AB PURPOSE: To determine whether the capacity of Langerhans cells (LCs) to abrogate ocular immune privilege can be suppressed by the topical application of interleukin-1 receptor antagonist (IL-1ra). METHODS: Cautery was applied to corneas of BALB/c mice on

day 0 to induce centripetal migration of LCs. Immune privilege was tested by the ability to induce anterior chamber-associated immune deviation (ACAID) to intracamerally injected soluble antigen 1 to 2 weeks after cautery application. The number of LCs was enumerated by immunofluorescent staining. In other experiments, freshly procured Thy-1-depleted epidermal cells, with or without LC depletion, were injected directly into virgin murine corneas before testing for ACAID. All test animals were randomized for treatment with either topical IL-1ra or placebo in a masked fashion for 1 to 2 weeks after induction of LC migration and before intracameral injection of antigen. RESULTS: Intracorneal injection of freshly procured LC-depleted epidermal cells into normal eyes failed to abrogate ACAID, whereas LC-containing cell populations uniformly led to loss of immune privilege ($P < 0.01$). Topical treatment with IL-1ra led to retention of the cauterized eyes' capacity for ACAID induction ($P < 0.01$) and to a profound (>80%) suppression of LC migration compared with untreated controls ($P < 0.01$). Additionally, topical IL-1ra treatment of eyes with intracorneally injected LCs preserved immune privilege and ACAID induction ($P < 0.001$). CONCLUSIONS: IL-1 mediates mechanisms of immunity in corneal inflammation that subvert the normal eye's immune privileged state. However, its antagonism with topical administration of IL-1ra preserves ocular immune privilege and ACAID through suppression of LC function.